Loss of sensitivity in appraising the relative saliency value of money in drug abusers is associated with disrupted activity in orbitofrontal cortex

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Orbitofrontal cortex (OFC) functional abnormalities in drug addiction have been previously documented. The OFC has also been implicated in salience attribution or relative reward processing in animal and human studies. We therefore used monetary reward graded for salience in a functional magnetic resonance imaging study to explore reward processing in drug addiction. Sixteen substance dependent individuals (SDI) (12 M; age 43±5 years; education 13±3 years) and 13 healthy controls (9 M; age 38±7 years; education 14±1 years) performed a forced-choice task under three blocked salience conditions: high money, low money, and no money. Subjects received up to $50 for their performance on this task. Results can be summarized as follows: 1) SDI rated low money as equivalent in subjective valence to high money, while controls did not. This suggests that perception [or processing] of relative reward salience is compromised in SDI; 2) the regional brain activation to relative money (higher money > lower money) was significantly blunted in the SDI when compared with controls and this included decreased activation in the OFC, anterior cingulate gyrus, and thalamus; 3) the activation of the OFC as a function of this relative monetary quantity (higher > lower) was associated with the subjective valence ratings, and specifically with the relative salience of money; and 4) mesencephalic brain regions (including substantia nigra and ventral tegmental area) were activated as a function of relative monetary quantity (higher > lower) in both SDI and controls, indicative of a dopaminergic response to relative money in all subjects that nevertheless was more attenuated in the SDI[was it less significant or were the means closer in SDI?]. Together, our results suggest that OFC functioning is disrupted in drug addiction in a manner that is specific to a compromised ability to code relative value of monetary (and possibly other non-drug-related) rewards. This lack of sensitivity to relative reward may reflect adaptations in the mesocortical dopamine system following chronic supraphysiological dopaminergic stimulation in drug addiction, and implicates the involvement of higher-order cognitive-emotional processes and the functional disruption of their underlying corticolimbic networks.